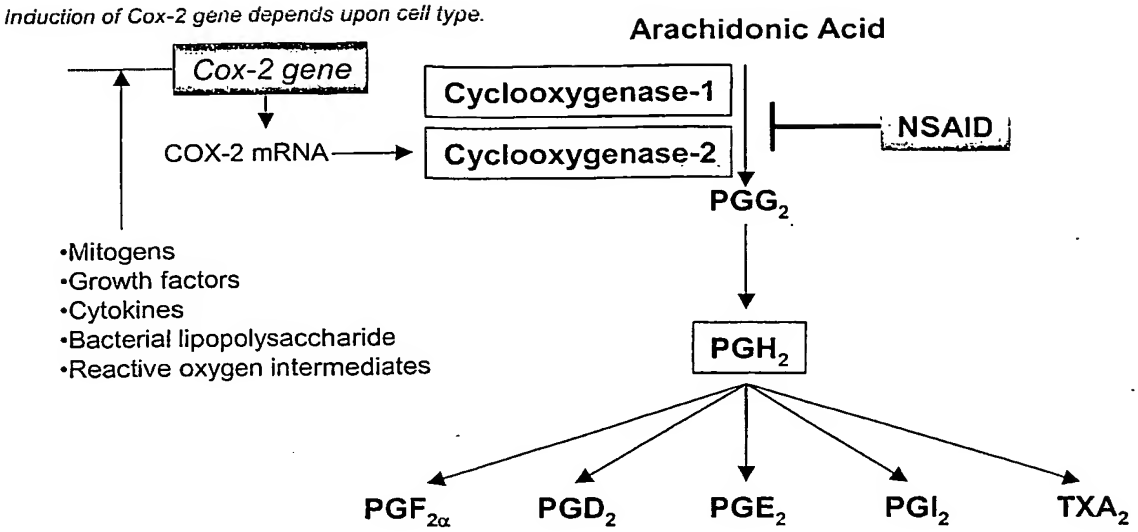

Induction of Cox-2 gene depends upon cell type.
Arachidonic Acid
Cox-2 gene
Cyclooxygenase-1
NSAID
COX-2 mRNA
Cyclooxygenase-2
PGG2
•Mitogens
•Growth factors
•Cytokines
•Bacterial lipopolysaccharide
•Reactive oxygen intermediates
PGH2
PGF2α
PGD2
PGE2
PGI2
TXA2
Array of eicosanoids produced depends upon cell type.
Cellular response is a function of intracellular and
extracellular receptors.

Figure 1

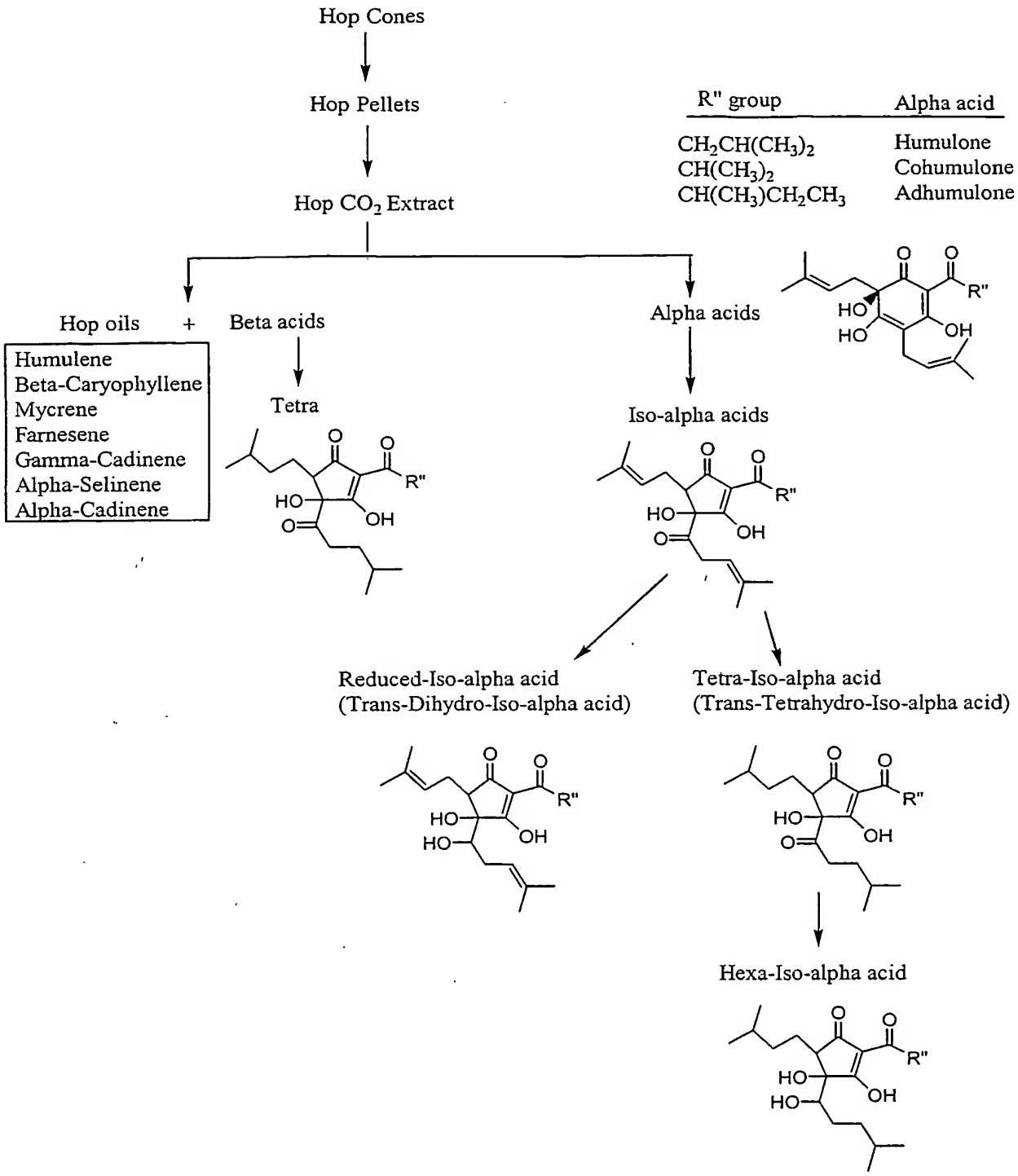
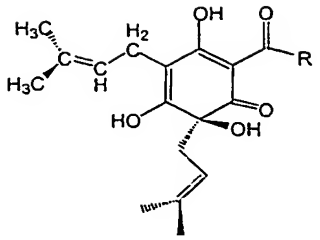
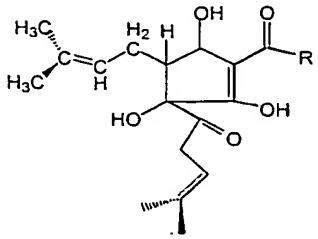

Hop Cones
Hop Pellets
Hop CO_2 Extract
R" group
Alpha acid
$CH_2CH(CH_3)_2$
Humulone
$CH(CH_3)_2$
Cohumulone
$CH(CH_3)CH_2CH_3$
Adhumulone
Hop oils
+
Beta acids
Alpha acids
Humulene
Beta-Caryophyllene
Mycrene
Farnesene
Gamma-Cadinene
Alpha-Selinene
Alpha-Cadinene
Tetra
Iso-alpha acids
Reduced-Iso-alpha acid
(Trans-Dihydro-Iso-alpha acid)
Tetra-Iso-alpha acid
(Trans-Tetrahydro-Iso-alpha acid)
Hexa-Iso-alpha acid

Figure 2

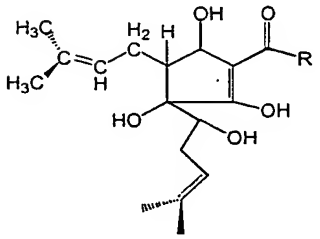
[A]



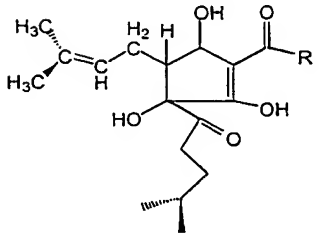
[B]



[C]



[D]



[E]

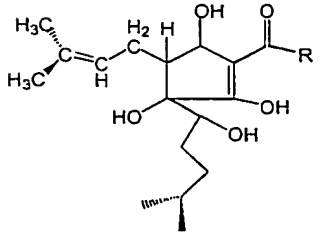
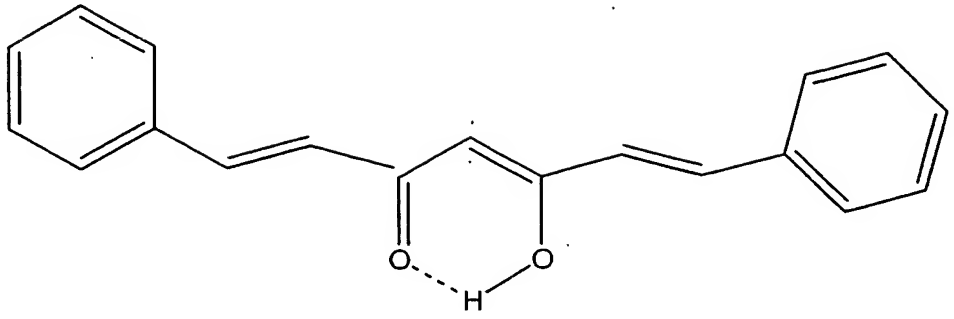


Figure 3

A



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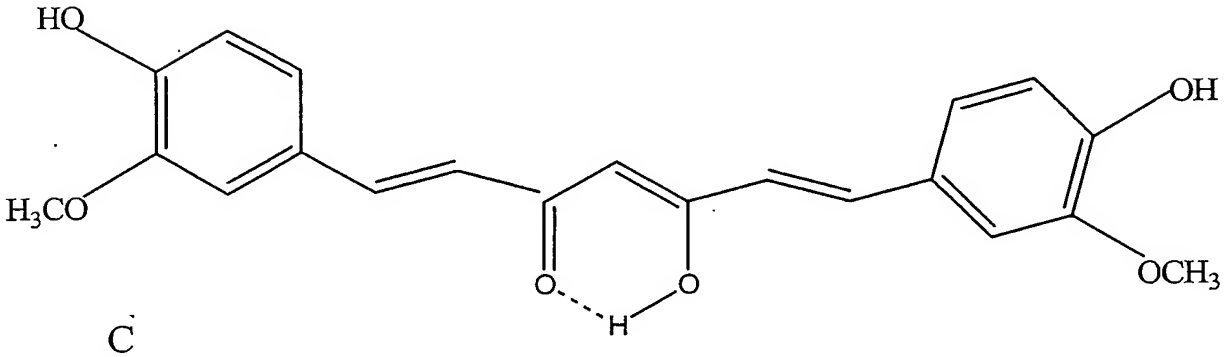

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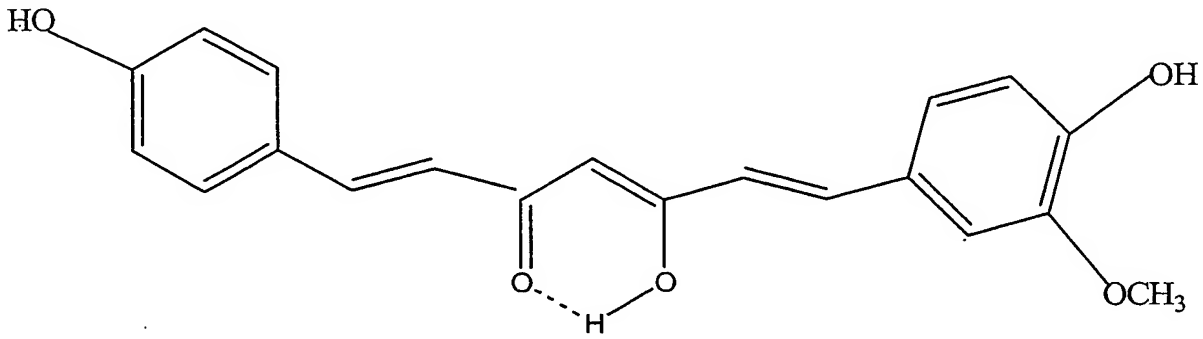
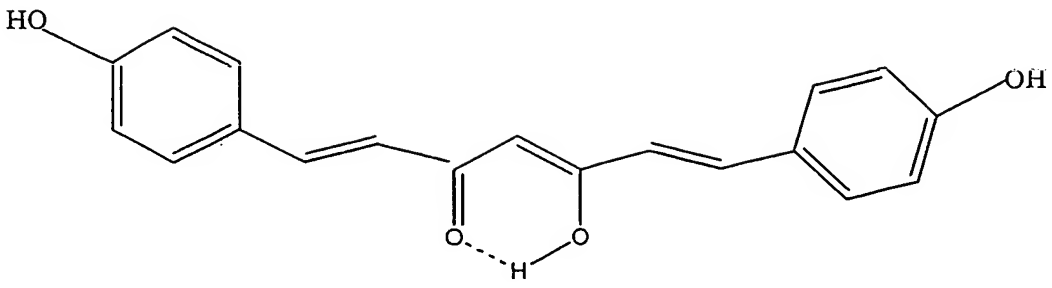


Figures 4 A-C

D



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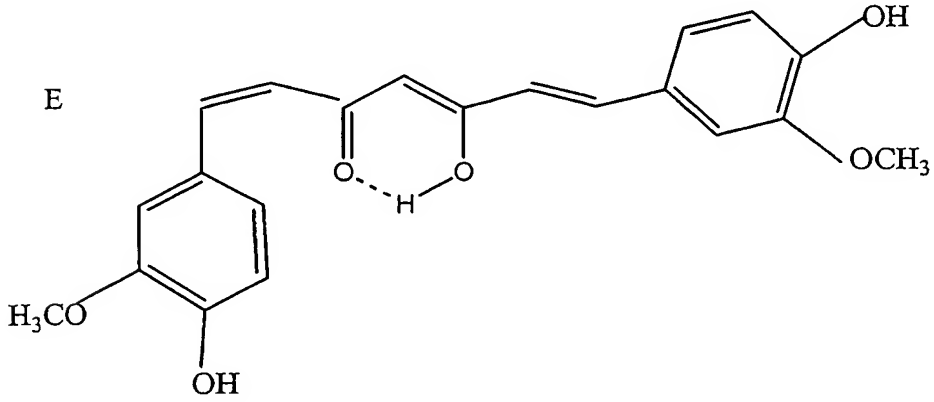
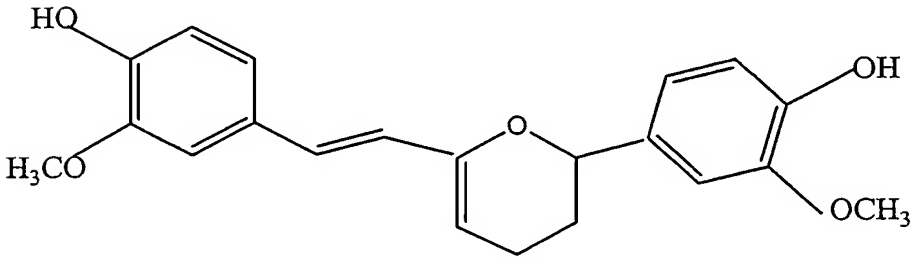
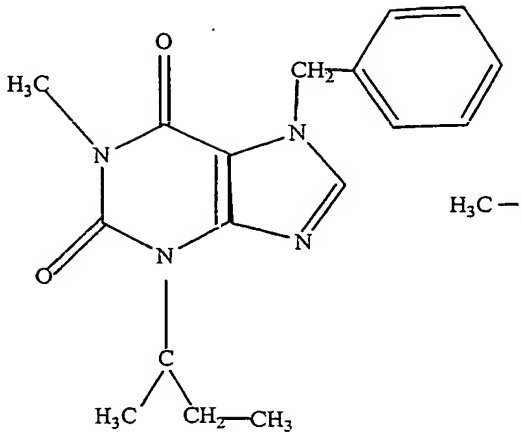


F



Figures 4 D-F

I



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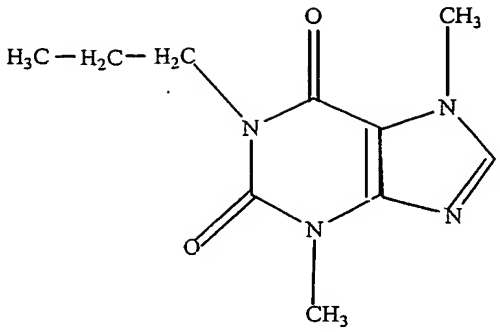
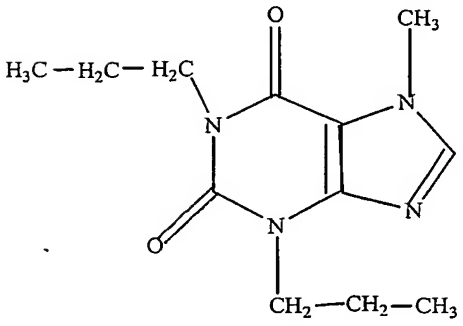
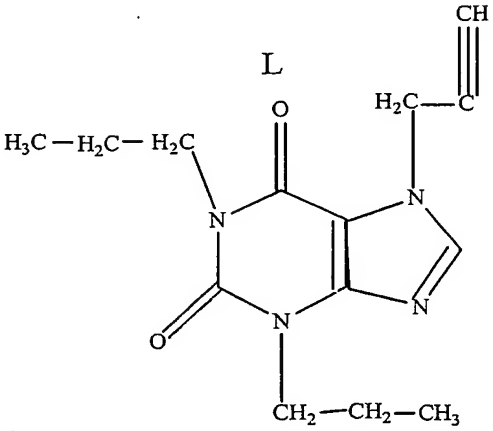


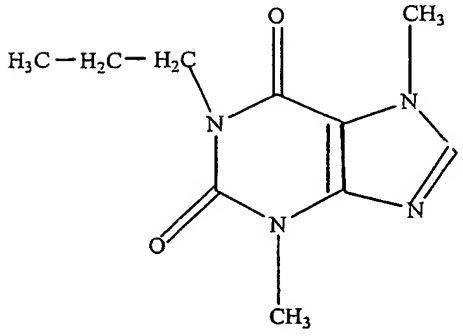
K



L



M



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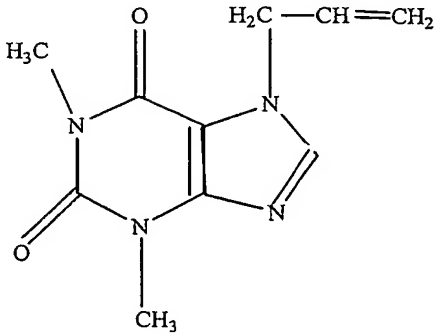
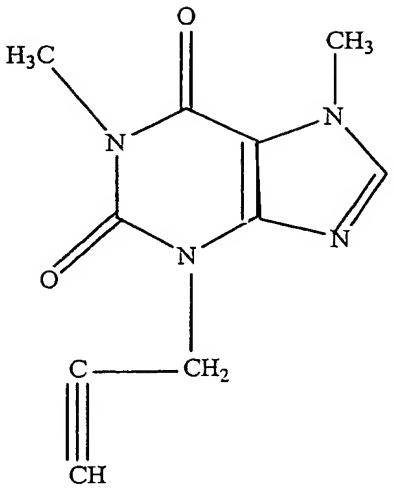


Figures 5I-N

E



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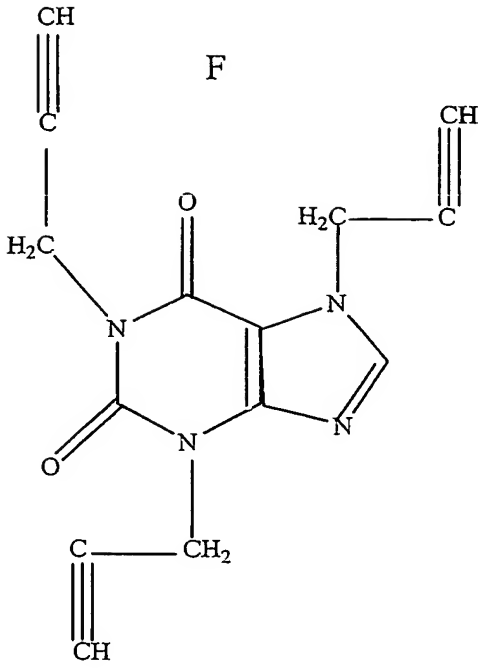

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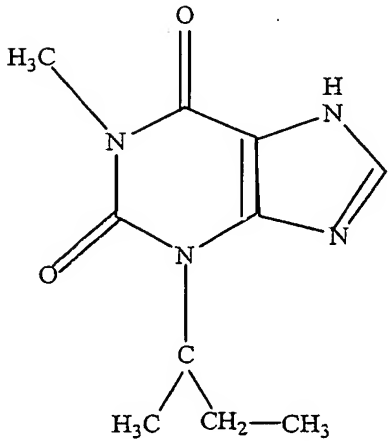

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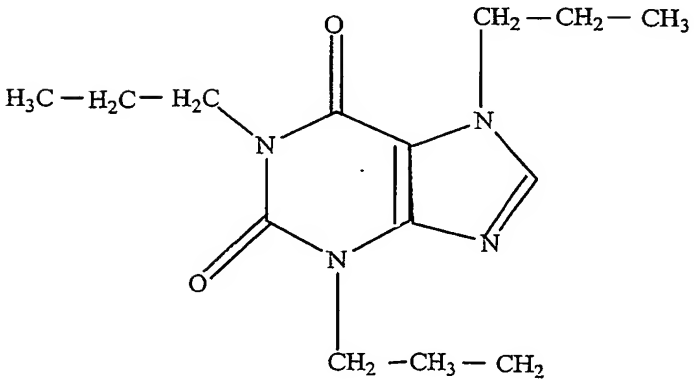
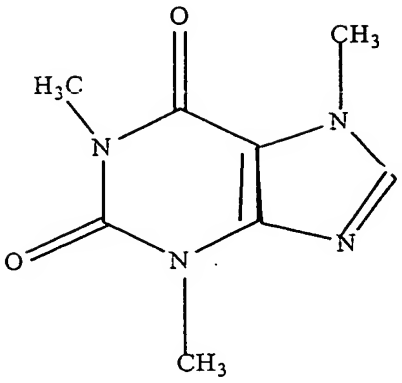
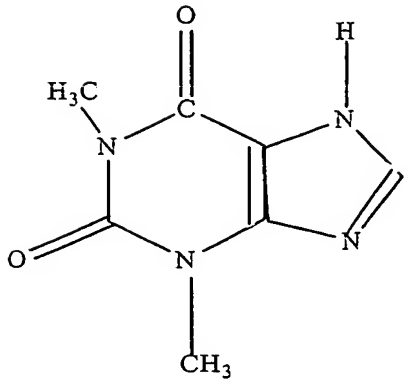


Figures 5 E-H

A



B



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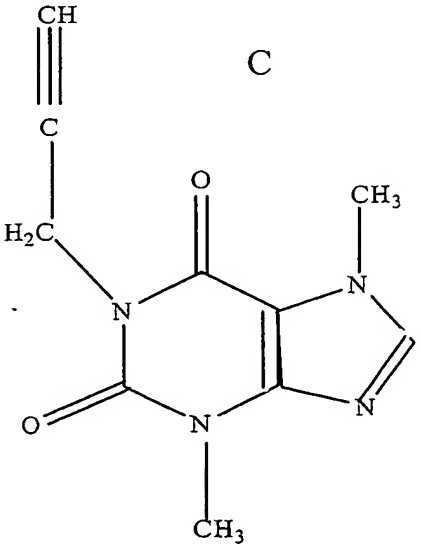

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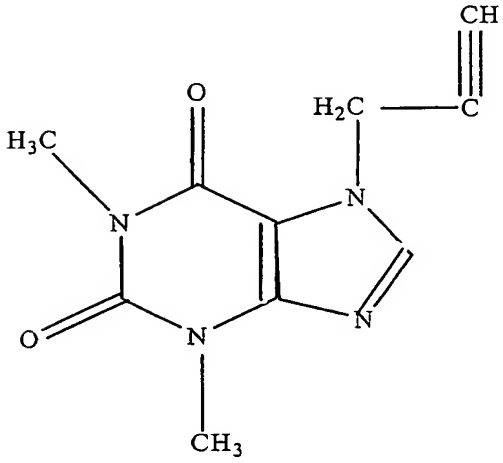

Figures 5 A-D

RIAA:Curcumin [100:1]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	68.336	0.01	0.000
0.05	28.842	0.04	0.000
0.10	14.609	0.10	0.001
0.15	9.589	0.18	0.002
0.20	6.984	0.28	0.003
0.25	5.376	0.40	0.004
0.30	4.277	0.55	0.006
0.35	3.475	0.73	0.007
0.40	2.862	1.0	0.010
0.45	2.375	1.2	0.012
0.50	1.979	1.6	0.016
0.55	1.649	2.0	0.020
0.60	1.369	2.6	0.026
0.65	1.127	3.4	0.034
0.70	0.916	4.6	0.046
0.75	0.729	6.3	0.063
0.80	0.562	9.0	0.090
0.85	0.409	14	0.139
0.90	0.269	25	0.247
0.95	0.137	63	0.629
1.00	0.031	495	4.950

Shaded area represents region of synergy

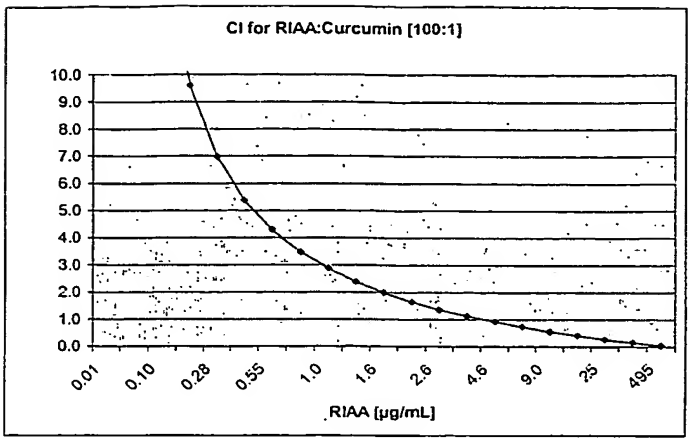

Figure 6A

RIAA:Curcumin [10:1]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	33.103	0.006	0.001
0.05	18.074	0.025	0.002
0.10	11.23	0.08	0.008
0.15	8.371	0.15	0.015
0.20	6.713	0.26	0.026
0.25	5.596	0.40	0.040
0.30	4.774	0.59	0.059
0.35	4.134	0.8	0.084
0.40	3.614	1.2	0.116
0.45	3.177	1.6	0.158
0.50	2.801	2.1	0.214
0.55	2.471	2.9	0.290
0.60	2.174	4.0	0.395
0.65	1.902	5.5	0.546
0.70	1.650	7.7	0.772
0.75	1.412	11	1.100
0.80	1.182	17	1.700
0.85	0.954	30	3.000
0.90	0.718	60	6.000
0.95	0.457	186	18.600
1.00	0.172	2266	226.600

Shaded area represents region of synergy

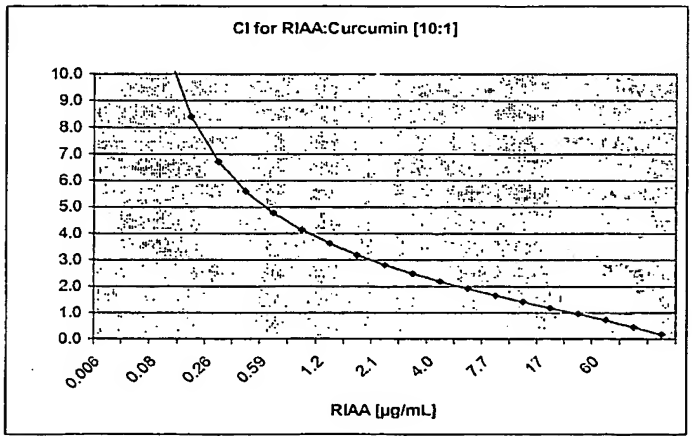

Figure 6B

RIAA:Curcumin [3:1]

Fa	CI	RIAA [µg/mL]	4708 [µg/mL]
0.02	0.073	0.000001	0.000
0.05	0.150	0.00020	0.000
0.10	0.266	0.0017	0.000
0.15	0.380	0.0070	0.002
0.20	0.497	0.018	0.004
0.25	0.622	0.041	0.010
0.30	0.756	0.085	0.021
0.35	0.904	0.17	0.041
0.40	1.069	0.31	0.077
0.45	1.256	0.56	0.14
0.50	1.472	1.0	0.25
0.55	1.726	1.8	0.45
0.60	2.031	3.2	0.81
0.65	2.410	6.0	1.5
0.70	2.894	12	2.9
0.75	3.546	24	6.0
0.80	4.479	56	14
0.85	5.957	153	38
0.90	8.732	584	146
0.95	16	5095	1274
1.00			

Shaded area represents region of synergy

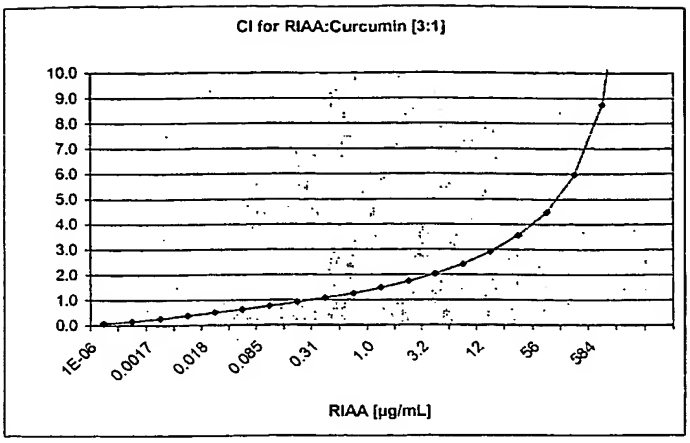

Figure 6C

RIAA:Curcumin [3:2]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	0.025	0.000004	
0.05	0.062	0.00008	0.000
0.10	0.129	0.0008	0.000
0.15	0.202	0.0032	0.001
0.20	0.285	0.0093	0.004
0.25	0.378	0.022	0.009
0.30	0.486	0.049	0.020
0.35	0.610	0.10	0.039
0.40	0.756	0.19	0.076
0.45	0.929	0.36	0.143
0.50	1.138	0.7	0.266
0.55	1.395	1.2	0.494
0.60	1.719	2.3	0.928
0.65	2.140	4.5	1.792
0.70	2.707	9.1	3.624
0.75	3.511	20	7.840
0.80	4.739	48	19.200
0.85	6.83	140	56.000
0.90	11	582	232.800
0.95	25	5830	2332.000
1.00	156		0.000

Shaded area represents region of synergy

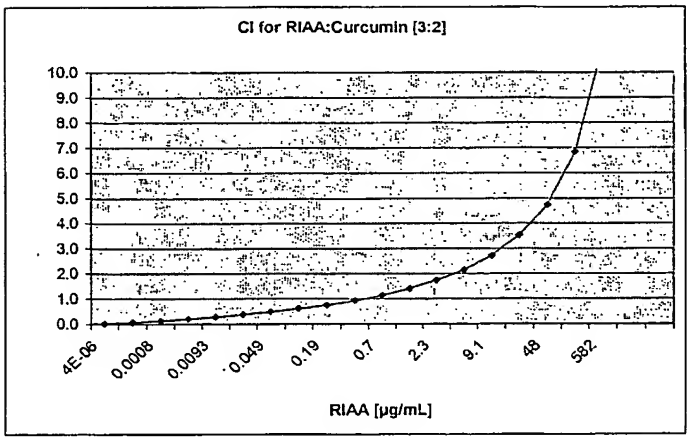

Figure 6D

RIAA:Curcumin [1:1]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	0.267	0.00004	0.00004
0.05	0.408	0.00047	0.00047
0.10	0.575	0.0032	0.0032
0.15	0.715	0.010	0.010
0.20	0.844	0.025	0.025
0.25	0.971	0.052	0.052
0.30	1.098	0.10	0.10
0.35	1.230	0.18	0.177
0.40	1.369	0.31	0.307
0.45	1.518	0.52	0.517
0.50	1.683	0.86	0.864
0.55	1.866	1.4	1.440
0.60	2.077	2.4	2.435
0.65	2.324	4.2	4.200
0.70	2.625	7.5	7.530
0.75	3.006	14.0	14.000
0.80	3.518	30.0	30.000
0.85	4.268	73	73.000
0.90	5.546	237	237.000
0.95	8.569	1600	1600.000
1.00			

Shaded area represents region of synergy

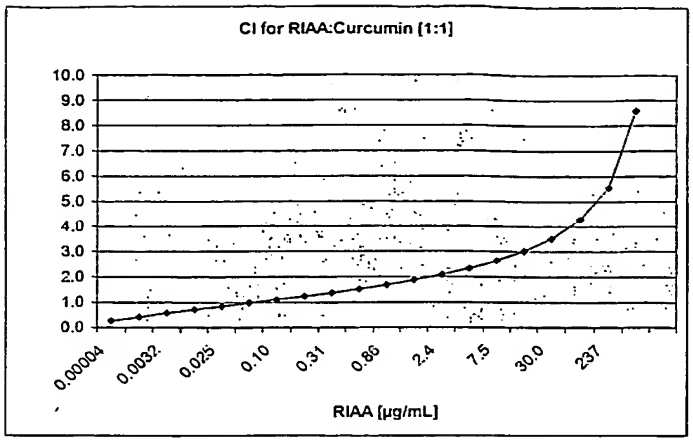

Figure 6E

RIAA:Curcumin [2:3]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	0.181	0.000026	0.00004
0.05	0.377	0.00040	0.00067
0.10	0.682	0.0034	0.0056
0.15	0.991	0.013	0.021
0.20	1.317	0.034	0.057
0.25	1.669	0.079	0.13
0.30	2.056	0.16	0.27
0.35	2.489	0.31	0.52
0.40	2.979	0.57	0.95
0.45	3.544	1.0	1.7
0.50	4.206	1.8	3.0
0.55	4.998	3.2	5.4
0.60	5.965	5.8	9.7
0.65	7.183	11	18
0.70	8.773	21	35
0.75	19.951	43	72
0.80			
0.85			
0.90			
0.95			
1.00			

Shaded area represents region of synergy

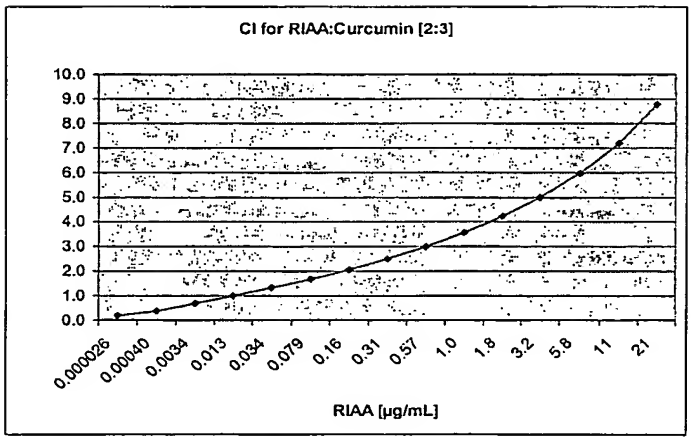

Figure 6F

RIAA:Curcumin [1:10]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	0.539	0.000037	0.00037
0.05	0.739	0.00032	0.0032
0.10	0.962	0.0018	0.018
0.15	1.140	0.0051	0.051
0.20	1.298	0.011	0.11
0.25	1.449	0.022	0.22
0.30	1.596	0.039	0.39
0.35	1.744	0.07	0.65
0.40	1.896	0.11	1.1
0.45	2.056	0.17	1.7
0.50	2.227	0.27	2.7
0.55	2.414	0.42	4.2
0.60	2.622	0.68	6.8
0.65	2.860	1.1	11
0.70	3.140	1.9	19
0.75	3.482	3.3	33
0.80	3.923	6.3	63
0.85	4.538	14	140
0.90	5.514	40	400
0.95			
1.00			

Shaded area represents region of synergy

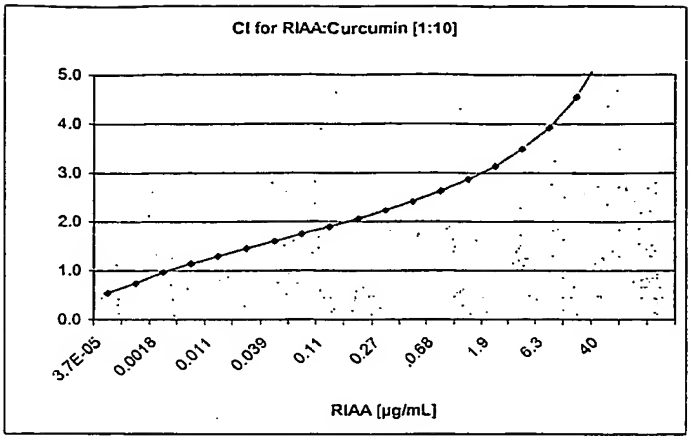

Figure 6G

RIAA:Curcumin [1:100]

Fa	CI	RIAA [µg/mL]	Curcumin [µg/mL]
0.02	0.773	0.0000082	0.00082
0.05	0.894	0.000055	0.0055
0.10	1.006	0.00025	0.025
0.15	1.083	0.00062	0.062
0.20	1.145	0.0012	0.12
0.25	1.200	0.0022	0.22
0.30	1.250	0.0037	0.37
0.35	1.297	0.0058	0.58
0.40	1.344	0.0089	0.89
0.45	1.389	0.013	1.3
0.50	1.436	0.020	2.0
0.55	1.484	0.030	3.0
0.60	1.536	0.045	4.5
0.65	1.591	0.069	6.9
0.70	1.652	0.11	11
0.75	1.723	0.18	18
0.80	1.807	0.32	32
0.85	1.916	0.64	64
0.90	2.070	1.6	160
0.95	2.347	7.2	720
1.00	3.1	197	19700

Shaded area represents region of synergy

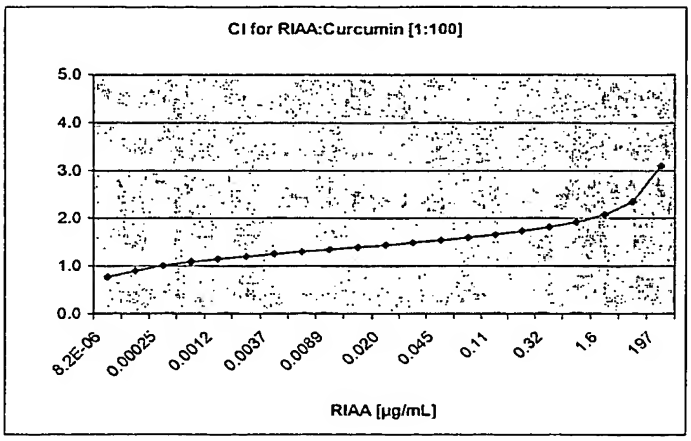

Figure 6H

RIAA:Caffeine [100:1]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	483000	0.010	0.000
0.05	23100	0.039	0.000
0.10	2104	0.11	0.0011
0.15	477	0.21	0.0021
0.20	156	0.34	0.0034
0.25	62	0.51	0.0051
0.30	28	0.72	0.0072
0.35	13	0.98	0.010
0.40	6.715	1.3	0.013
0.45	3.481	1.8	0.018
0.50	1.829	2.3	0.023
0.55	0.961	3.1	0.031
0.60	0.498	4.1	0.041
0.65	0.251	5.5	0.055
0.70	0.121	7.5	0.075
0.75	0.054	11	0.11
0.80	0.021	16	0.16
0.85	0.007	26	0.26
0.90	0.002	49	0.49
0.95	0.000	138	1.4
1.00	0.000	1360	14

Shaded area represents region of synergy

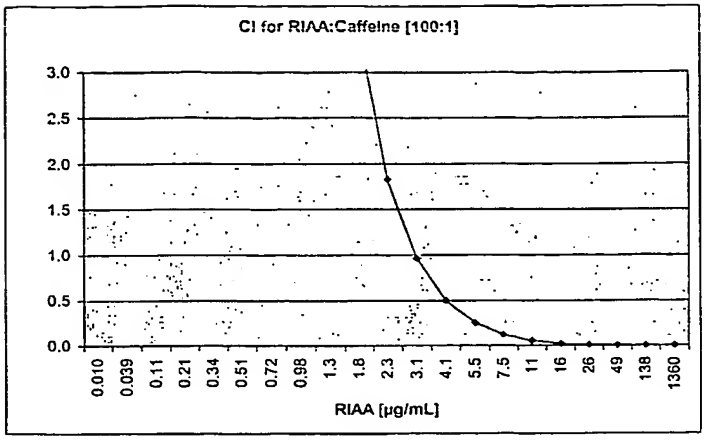

Figure 7A

RIAA:Caffeine [10:1]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	25	0.00000054	0.000000
0.05	14	0.000023	0.000002
0.10	8.673	0.0005	0.000045
0.15	6.514	0.0029	0.00029
0.20	5.252	0.011	0.0011
0.25	4.396	0.036	0.0036
0.30	3.764	0.097	0.010
0.35	3.270	0.24	0.024
0.40	2.866	0.56	0.056
0.45	2.527	1.3	0.13
0.50	2.233	2.8	0.28
0.55	1.974	6.3	0.63
0.60	1.742	14.0	1.4
0.65	1.529	33.0	3.3
0.70	1.330	82.0	8.2
0.75	1.142	222	22
0.80	0.961	697	70
0.85	0.781	2787	279
0.90	0.596	17533	1753
0.95	0.393	341940	34194
1.00	0.195	242070000	

Shaded area represents region of synergy

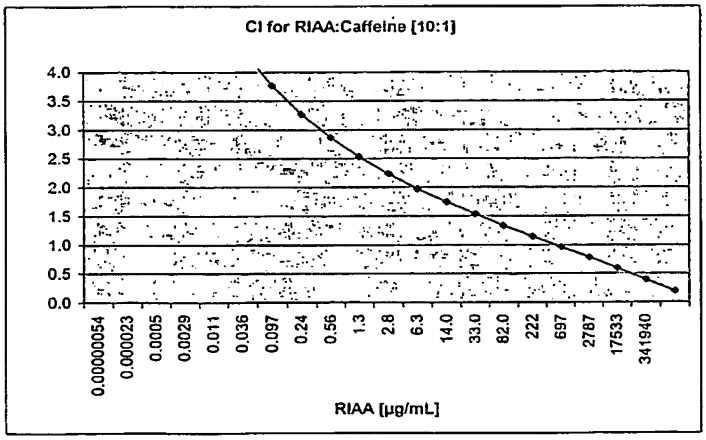

Figure 7B

RIAA:Caffeine [3:1]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	60	0.0000013	0.000000
0.05	22.000	0.000038	0.000010
0.10	10.324	0.0005	0.000
0.15	6.380	0.0028	0.001
0.20	4.442	0.010	0.002
0.25	3.296	0.027	0.007
0.30	2.540	0.065	0.016
0.35	2.006	0.15	0.037
0.40	1.609	0.31	0.078
0.45	1.303	0.65	0.16
0.50	1.060	1.3	0.33
0.55	0.863	2.7	0.67
0.60	0.700	5.6	1.4
0.65	0.564	12	3.0
0.70	0.448	27	6.8
0.75	0.348	66	17
0.80	0.262	182	46
0.85	0.187	627	157
0.90	0.121	3245	811
0.95	0.064	46124	11531
1.00	0.023	16236000	

Shaded area represents region of synergy

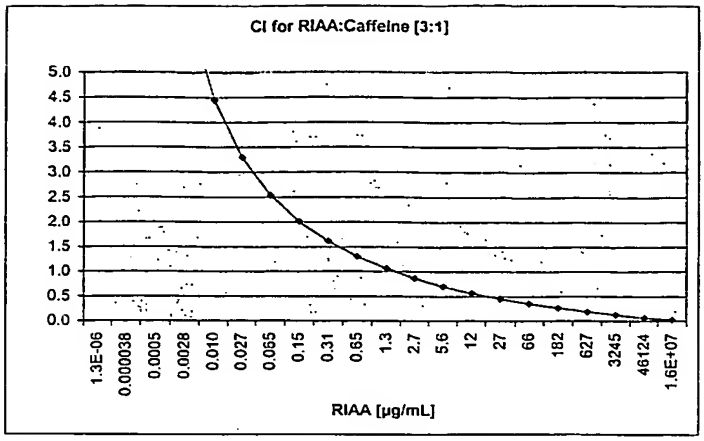

Figure 7C

RIAA:Caffeine [3:2]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	538000	0.012	0.005
0.05	21100	0.036	0.014
0.10	1640	0.086	0.034
0.15	337	0.15	0.059
0.20	103	0.22	0.089
0.25	39	0.31	0.124
0.30	16	0.42	0.167
0.35	7.534	0.55	0.218
0.40	3.645	0.70	0.281
0.45	1.818	0.89	0.357
0.50	0.921	1.1	0.452
0.55	0.467	1.4	0.572
0.60	0.234	1.8	0.728
0.65	0.114	2.3	0.920
0.70	0.053	3.1	1.240
0.75	0.0230	4.1	1.640
0.80	0.009	5.8	2.304
0.85	0.0030	8.7	3.472
0.90	0.0010	15	6.000
0.95	0.000062	36	14.400
1.00	0.00000058	251	100.400

Shaded area represents region of synergy

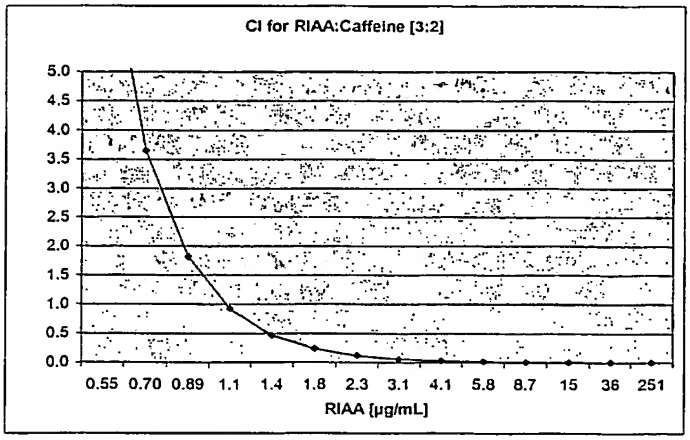

Figure 7D

RIAA:Caffeine [1:1]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	0.176	0.0000000038	0.00000
0.05	0.209	0.00000035	0.00000
0.10	0.241	0.000013	0.0000
0.15	0.263	0.00011	0.00011
0.20	0.281	0.00060	0.00060
0.25	0.298	0.0024	0.0024
0.30	0.313	0.0079	0.0079
0.35	0.328	0.024	0.024
0.40	0.343	0.065	0.065
0.45	0.359	0.17	0.17
0.50	0.376	0.45	0.45
0.55	0.394	1.2	1.2
0.60	0.415	3.2	3.2
0.65	0.438	8.7	8.7
0.70	0.467	26	26
0.75	0.504	86	86
0.80	0.554	341	341
0.85	0.632	1805	1805
0.90	0.779	16460	16460
0.95	1.206	584650	584650
1.00	5.041	1556200000	1556200000

Shaded area represents region of synergy

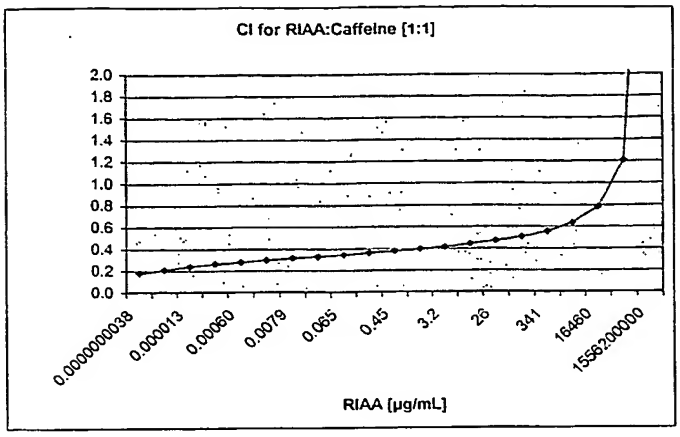

Figure 7E

RIAA:Caffeine [2:3]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	0.001	$1.5*10^{-11}$	$2.5*10^{-11}$
0.05	0.003	$5.1*10^{-9}$	$8.5*10^{-9}$
0.10	0.010	$5.2*10^{-7}$	$8.7*10^{-7}$
0.15	0.021	$9.1*10^{-6}$	$15*10^{-6}$
0.20	0.037	$7.8*10^{-5}$	$13*10^{-5}$
0.25	0.058	0.00046	0.00077
0.30	0.087	0.00217	0.0036
0.35	0.125	0.01	0.01
0.40	0.177	0.03	0.06
0.45	0.247	0.1	0.2
0.50	0.343	0.4	0.7
0.55	0.478	1.4	2.3
0.60	0.673	4.9	8.2
0.65	0.966	18	30
0.70	1.428	76	127
0.75	2.215	357	595
0.80	3.702	2105	3508
0.85	7.037	18069	30115
0.90			
0.95			
1.00			

Shaded area represents region of synergy

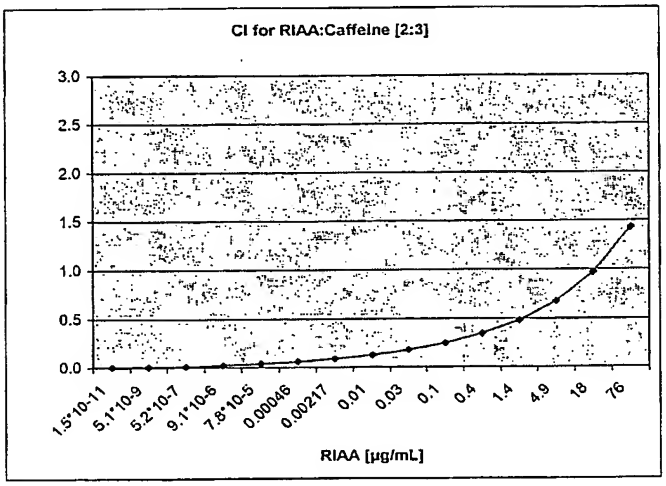

Figure 7F

RIAA:Caffeine [1:10]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	0.958	$2.1*10^{-8}$	$2.1*10^{-7}$
0.05	0.542	$8.9*10^{-7}$	$8.9*10^{-6}$
0.10	0.351	$1.74*10^{-5}$	$1.74*10^{-4}$
0.15	0.272	0.00011	0.0011
0.20	0.227	0.00044	0.0044
0.25	0.197	0.0014	0.014
0.30	0.175	0.0037	0.037
0.35	0.159	0.01	0.09
0.40	0.147	0.02	0.2
0.45	0.137	0.05	0.5
0.50	0.128	0.11	1.1
0.55	0.122	0.24	2.4
0.60	0.117	0.54	5.4
0.65	0.113	1.3	13
0.70	0.110	3.2	32
0.75	0.109	8.6	86
0.80	0.110	27.0	270
0.85	0.113	107	1070
0.90	0.122	676	6760
0.95	0.148	13202	132020.000
1.00	0.258	$9.4*10^{6}$	$9.4*10^{7}$

Shaded area represents region of synergy

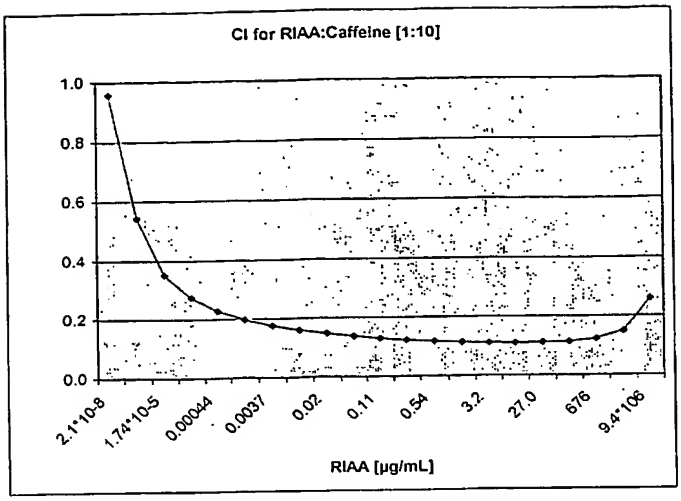

Figure 7G

RIAA:Caffeine [1:100]

Fa	CI	RIAA [µg/mL]	Caffeine [µg/mL]
0.02	0.003	$5.7*10^{-11}$	$5.7*10^{-9}$
0.05	0.005	$6.7*10^{-9}$	$6.7*10^{-7}$
0.10	0.008	$2.9*10^{-7}$	$2.9*10^{-5}$
0.15	0.013	$2.9*10^{-6}$	$2.9*10^{-4}$
0.20	0.017	$1.7*10^{-5}$	$1.7*10^{-3}$
0.25	0.023	$7.1*10^{-5}$	$7.1*10^{-3}$
0.30	0.031	0.00025	0.025
0.35	0.040	0.0008	0.08
0.40	0.051	0.0023	0.23
0.45	0.066	0.0065	0.65
0.50	0.085	0.018	1.8
0.55	0.110	0.049	4.9
0.60	0.143	0.14	13.7
0.65	0.190	0.40	40.1
0.70	0.259	1.3	126
0.75	0.365	4.5	446
0.80	0.543	19	1900
0.85	0.882	109	10900
0.90	1.693	1116	111600
0.95		47705	4770500
1.00			

Shaded area represents region of synergy

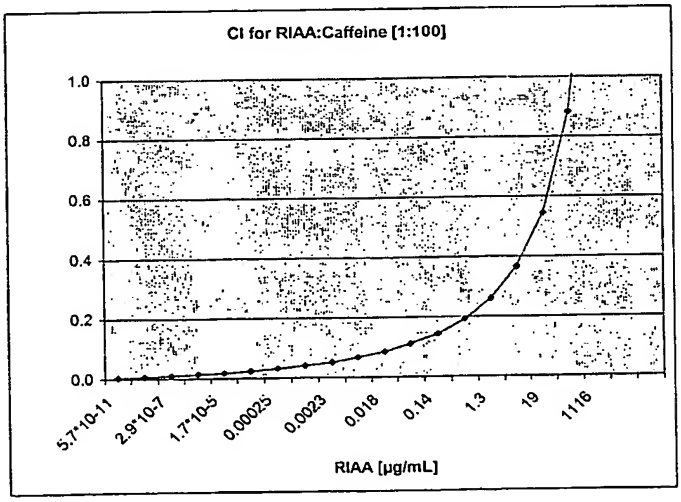

Figure 7H